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10/797,606	03/11/2004	Masato Kurokawa	042190	3867

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EXAMINER	
GUDIBANDE, SATYANARAYAN R	
ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/797,606	KUROKAWA ET AL.	
	Examiner	Art Unit	
	Satyanarayana R. Gudibande	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) *8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Prosecution on the merits of this application is reopened after final rejection on claim 1-8 considered unpatentable for the reasons indicated below:

The claims are unpatentable over prior art of record under obviousness statute (please see the modified obviousness rejection below) and the claims are unpatentable over 35 USC 112 first paragraph for lack of written description as shown below.

Election/Restrictions

Applicant's election of Arg-Gly-Asp and auxiliary amino acid sequence of Gly-Ala-Gly-Ala-Gly-Ser and polyalkylenepolyamine in their response to election restriction filed on 10/7/05 was acknowledged on 1/29/05 in a non-final office action.

Claims 1-8 are pending.

Claims 8 have been withdrawn from further consideration as being drawn to non-elected invention.

Claims 9 and 10 have been canceled.

Claims 1-7 are examined on the merit.

Applicant's remarks and amendment to claims in the response filed on 10/9/07 has been acknowledged and entered.

Any objections and rejections made in the office action dated 7/12/07 and not specifically mentioned here are considered withdrawn.

Claim Objections

Applicant's response to claim objection has been acknowledged. Applicants have amended claim 1 to incorporate the limitation of claim 10 narrowing the scope of the claim from chemical bonding to recite covalent boding. However, upon further consideration, the narrowing of the scope of claim 1 introduced new issues and hence the rejection under the obviousness statute has been modified as it appears below.

Rejoinder of withdrawn claim (claim 8)

Since the claims 1-7 as amended are not in condition for allowance, the request for rejoinder of the method claim 8 will be considered if and when the product claims 1-7 will become suitable for allowance.

Maintained Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Please note: The rejection under 35 USC 103(a) has been modified as it appears below. Applicant's remarks filed 10/9/07 have been addressed following the rejection.

Claims 1-7 remain rejected under 35 U.S.C. 103(a) as being unpatentable over US patent 6,184,348 B1 issued to Ferrari, et al., in view of US 5,916,585 issued to Cook, et al., as stated in our office action dated 10/20/06 for claims 1-7 and 9.

In the instant application, applicants claim a wound dressing for accelerating epidermal regeneration which **comprises a polypeptide (P)** having at least one species of (X) for e. g., RGD and an auxiliary amino acid (Y) for e. g., GAGAGS peptides, a polyalkylenepolyamine having a molecular weight of 2000 to 60,000 d, and a sheet (s) being at least one member selected from the group consisting of polyolefin, polyurethane, polyester, polyamide, polystyrene and silicone resin, wherein the polypeptide (P) and the sheet (S) are bonded by a covalent bonding.

Ferrari, et al., discloses the composition of the peptide copolymer of RGD and GAGAGS peptides in claims 4-6 of US 6,184,348 B1 (column 141, lines 8-29). The reference also teaches that the aforementioned copolymers can be deposited onto other substrates and materials for a

cell-binding surface. Such coated materials or substrates are used for wound dressing that promotes enhanced healing (Column 28, lines 35-45). The reference of Ferrari, does not teach the use of polyalkylenepolyamine or polyarylenepolyamine matrices.

Cook, et al discloses materials and methods for the immobilization of bioactive species onto biodegradable polymers. The invention is directed to hydrophobic degradable polymeric material having at least one surface thereof rendered hydrophilic by cross-linking a hydrophilic polymer layer. The bioactive species are either reversibly immobilized or cross-linked with the cross linking agent that cross-links the hydrophilic polymer with the hydrophobic biodegradable polymeric material (abstract). Cook, et al., discloses suitable polymeric material that forms the biodegradable hydrophobic surface as polyesters of oxalic acid and polyurethanes (bridging paragraph of columns 9 and 10 and claim 4) which is the sheet (s) of the instant application. This meets the limitations of claim1 and 9. The biodegradable hydrophilic surfactant layer comprises of polyethyleneimine and other polyalkylenepolyamines (claim 7, 25 and 30), meeting the limitations of claims 1 and 7. The reference also discloses the variety of bioactive species immobilized on the biodegradable polymeric material that includes tripeptide Arg-Gly-Asp (column 6, line 60) meeting the limitations of claim 1. Example 18 of the reference uses the polymeric material of the invention for a surgical mesh made up of PGA:PLA fiber mesh and an antimicrobial drug gentamycin reversibly cross-linked to polyethyleneimine (PEI) to treat surgical wounds to prevent infection (column 21, example 18).

The references of Ferrari and Cook also do not teach covalent bonding between the peptide (P) and the polymer sheet (S).

It would have been obvious to one of ordinary skill in the art to modify the teachings of Ferrari and Cook to design a wound dressing for accelerated epidermal regeneration. Ferrari, teaches the composition of the peptides ARG and GAGAGS that can be used as a coating on materials or substrates used for wound dressing. Cook describes the material and methods for immobilization of bioactive species onto biodegradable polymers. The motivation to combine teachings of Ferrari and Cook was available in Ferrari as the reference teaches that the peptide composition may be coated on a matrix of woven fabric or film or membrane and used as wound dressing to promote enhanced healing due to attachment of cells involved in the healing and Cook describes such a method to immobilize bioactive materials onto biodegradable polymeric matrix. There would have been reasonable expectation of success in the present instance to combine the teachings of Ferrari and Cook to design a wound dressing composition for rapid epidermal regeneration because such a method and use of polymeric matrix has been disclosed by the references. Ferrari teaches the peptides that can be used as bioactive ingredients Cook teaches the polymeric matrix composed of polyurethane sheet with hydrophilic layer of polyethyleneimine for the adsorption or cross-linking of the bioactive peptides to form the wound dressing. Cook also successfully teaches a surgical mesh made up of PGA:PLA fiber mesh and an antimicrobial drug gentamycin reversibly cross-linked to polyethyleneimine (PEI) to treat surgical wounds to prevent infection.

It has been held that under *KSR* that "obvious to try" may be an appropriate test under 103. The Supreme Court stated in *KSR* When there is motivation "to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good

reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, ___, 82 USPQ2d 1385, 1397 (2007).

The "problem" facing those in the art was attachment of polypeptide (P) to the polymer matrix (S) and there were a limited number of methodologies available to do so, for example ionic interaction, hydrophobic interaction, physical adsorption, reversible cross-linking and covalent bonding. Ferrari teaches that the peptide composition may be coated on a matrix (physical adsorption or ionic interaction) of woven fabric or film or membrane and used as wound dressing to promote enhanced healing due to attachment of cells involved in the healing and Cook describes a method to immobilize bioactive materials onto biodegradable polymeric matrix. In each of the cited references, the association of peptide in with the matrix would be one of freely diffusing in the (dressing) matrix. The skilled artisan would have had reason to try methodologies that would adhere the peptide with the matrix more tightly via a covalent bonding with the reasonable expectation that the peptide is available at the wound site instead of freely diffusing in the matrix and one would be would be successful in designing such a matrix wherein the peptide is bound to the matrix via covalent bonding. Thus, the covalent bonding of the peptide with the matrix "the product not of innovation but of ordinary skill and common sense," leading us to conclude that the wound dressing wherein the peptide is covalently bound to the matrix is not patentable as it would have been obvious.

Therefore, the invention as a whole is clearly a prima-facie obvious to one skilled in the art at the time the invention was made to combine the teachings of Ferrari and Cook to formulate a wound dressing composition.

Response to applicant's arguments

Applicants argue that Ferrari discloses the instant invention without the polyalkylenepolyamine and a polyurethane sheet and office relies on Cook reference to provide these teachings. Since applicants have amended the claims to incorporate the limitations of claim 10 in to claim 1, the rejection under 35 USC 103 is moot.

Applicant's arguments with respect to claims 1-7 have been considered but are moot in view of the new ground(s) of rejection. The rejection under 35 USC 103 has been modified as shown above to rebut the arguments of applicants.

New grounds of rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the instant application, applicants claim a wound dressing for accelerating epidermal regeneration which **comprises a polypeptide (P)** having at least one species of (X) for e. g., RGD and an auxiliary amino acid (Y) for e. g., GAGAGS peptides, a polyalkylenepolyamine having a molecular weight of 2000 to 60,000 d, and a sheet (s) being polyurethane wherein the polypeptide (P) and the sheet (S) are bonded by a covalent bonding.

The MPEP clearly states that the purpose of the written description is to ensure that the inventor had possession of invention as of the filing date of the application, of the subject matter later claimed by him. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir.1997). The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the application. These include, "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed invention is sufficient" MPEP 2163.

In the instant application, applicants claim a wound dressing comprising a polypeptide (P) that in turn comprises of at least one species of peptide (X) and an auxiliary amino acid sequence (Y). The polypeptide (P) as recited in the claim represents any and all peptides that comprises of the peptide (X) and peptide (Y). The specification provides a disclosure on the definition of polypeptide (P) that encompasses a polypeptide of molecular weight 1000 to 1,000,000 (page 8, line 19-20). The definition of peptide (P) in the specification (page 4, line 7 to page 10, line 22) provides a very broad definition that encompasses multitude of peptide sequences that comprises of peptide sequence (X) and (Y) in an undefined sequence of unknown length. The peptide (P) as recited in the claim 1 does not provide structural features of the peptide (partial or full) such as nature of association of peptide (X) and peptide (Y) that make up polypeptide (P). In terms of specific examples of polypeptide (P), the specification provides ProNectin F (page 24, example 1), ProNectin F2 (page 26, example 2), ProNectin F3 (page 26, example 3), ProNectin L (page 27, example 4). However, the composition of each of these ProNectins and the molecular weight disclosed for each of these proNectins indicates that the polypeptide in each case is not just limited to the composition of the peptides (X) and (Y) and contains unknown structural features that is neither well defined in the specification nor recited in the claims, for e.g., ProNectin F on page 24 has been defined as "ProNectin F (product of Sanyo Chemical Industries, Ltd.), which contains the Arg Gly Asp (RGD)sequence (1) and the $(Gly\ Ala\ Gly\ Ala\ Gly\ Ser)_9$ sequence (8) each in the number of about 13 and has a Mw of about 110,000 d". If the average molecular weight of each amino acid is ~110 daltons (d), the tripeptide RGD corresponds to 330 and if the ProNectin F has 13 of these RGD peptides, then the molecular weight corresponding to RGD peptide will be 4290 d, in a similar way, the

molecular corresponding to 13 repeats of (Gly Ala Gly Ala Gly Ser)$_9$ will be 77,220 d. The total molecular weight of the ProNectin F will be ~81,510 d. However, the disclosed molecular weight of the ProNectin F is ~110,000 d. Hence there is a marked discrepancy in molecular weight of the ProNectin F (polypeptide P) between the disclosed sequence and the actual molecular weight of the polypeptide. Further, the definition of polypeptide (P) that encompasses a polypeptide of molecular weight 1000 to 1,000,000 (page 8, line 19-20) as mentioned above. Therefore, the minimum number of amino acid residues in a peptide in a peptide with a MW of 1000 d is 9 amino acids and for peptide with a MW of 1,000,000 d, it would be 9090 residues. According claim 2, the minimal amino acid sequence (X) is present in the number 3 to 50 and according to claim 3, the auxiliary amino acid sequence (Y) is present in the number 2-51. If the polypeptide (P) has a structure that has (X) and (Y) peptide moieties bonded to each other in an alternating fashion (according to claim 4), then a minimum molecular weight of 1000 d for the polypeptide (P) is irrelevant because, such a peptide comprising minimum 3 of peptide (X) and minimum 2 of peptide (Y) is not possible as it would exceed the minimum molecular weight limitations disclosed in the specification as per the recited claims. If the peptides represent 'any peptide sequence', then there are 9^{20} sequences for the minimum molecular weight and 9090^{20} sequences for the molecular weight 1,000,000 comprising only the 20 naturally occurring amino acid residues.

Moreover, claim 2 recite a limitation, "epidermal regeneration-accelerating minimal amino acid sequence (X) is in the number 3 to 50 in each molecule of the polypeptide (P)". It is unclear from the recitation whether the number 3 to 50 represents the number repeat units of the polypeptide (X) or it is the length of the peptide sequence. If it is the length of the peptide

sequence with repeated RGD, then, a length other than the multiple of 3 does not have adequate support in the instant application.

Claim 3 recite a limitation, "auxiliary amino acid sequence (Y) is in the number 2 to 51 in each molecule of the polypeptide (P)". It is unclear from the recitation whether the number 2 to 51 represents the number repeat units of the polypeptide (Y) or it is the length of the peptide sequence. If it is the length of the peptide sequence with repeated IKVAV or YIGSR or GAGAGS, then, a length other than the multiple of 5 or 6 does not have adequate support in the instant application, i.e. a length of 27 amino acids is not supported in the specification.

This leads to the conclusion that the identity of the polypeptide P, has neither been disclosed in the specification nor recited in the claim as presented in the instant application as per the above discussion. Since the specification falls short of a clear disclosure with respect to the nature of the polypeptide P as per the afore-described analysis, the claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2 and 3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 recite a limitation, "epidermal regeneration-accelerating minimal amino acid sequence (X) is in the number 3 to 50 in each molecule of the polypeptide (P)". It is unclear from the recitation whether the number 3 to 50 represents the number repeat units of the polypeptide (X) or it is the length of the peptide sequence. If it is the length of the peptide sequence with repeated RGD, then, a length other than the multiple of 3 does not have adequate support in the instant application.

Claim 3 recite a limitation, "auxiliary amino acid sequence (Y) is in the number 2 to 51 in each molecule of the polypeptide (P)". It is unclear from the recitation whether the number 2 to 51 represents the number repeat units of the polypeptide (Y) or it is the length of the peptide sequence. If it is the length of the peptide sequence with repeated IKVAV or YIGSR or GAGAGS, then, a length other than the multiple of 5 or 6 does not have adequate support in the instant application, i.e. a length of 27 amino acids is not supported in the specification.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyanarayana R. Gudibande whose telephone number is 571-272-8146. The examiner can normally be reached on M-F 8-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Satyanarayana R. Gudibande, Ph.D.
Art Unit 1654

11/7/07
ANISH GUPTA
PRIMARY EXAMINER